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EXAMINER	
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1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,747	KOBAYASHI ET AL.	
	Examiner	Art Unit	
	NARAYAN K. BHAT	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,21-25 and 27-34* is/are pending in the application.

4a) Of the above claim(s) *8-16 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 17, 19, 21-25 and 27-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This office action is written in reply to the Applicant's correspondence filed April 12, 2010. Applicant's amendment requiring observing the individual chain molecules immobilized uprightly on the plastic substrate surface necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.**

Claim Status

2. This action is in response to papers filed on April 12, 2010. Claims 1-19, 21-25 and 27-34 are pending in this application. Claims 1 and 19 are amended. Claim 26 is cancelled. The claim amendments have been reviewed and entered. Applicant's arguments filed April 12, 2010 have been fully considered and addressed following the rejections.

3. Claims 8-16 and 18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and Applicant's timely traversed election requirement made final on June 12, 2007.

4. Claims 1-7, 17, 19, 21-25 and 27-34 are under examination.

Note to Applicants

5. Applicants in their amended claim listing and remarks filed on April 12, 2010, identified Application as 10/533,747 instead of 10/553,747. Acknowledgement of the typographical error regarding said application number in the next reply is greatly appreciated.

Priority

6. In view of the claimed priority to application Japan 2003-114836 filed in Japan and certified English translation of the application on April 12, 2010, the effective filing date for the instant claims is April 18, 2003. Based on the effective filing date for the instant claims and Applicant's arguments that the reference of Henderson et al (USPGPUB 2003/0186311, filing date April 30, 2003) is not available as prior art (Remarks, pgs. 10 and 11). Applicant's arguments are persuasive. The reference of Henderson is withdrawn from further considerations.

Claim Objections -Duplicate claim warning

7. Previous objection to the claim 26 is withdrawn in view of cancellation of the said claim.

Claim Rejections - 35 USC § 112

8. The previous rejections of claim 19 and its dependent claims 21-27 and 33-34 under 35 USC 112 Second Paragraph are withdrawn in view of providing proper antecedent basis for "plastic" in claim 19.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-7, 17, 28-30 and 32 are rejected under 35 U.S.C. 102(e) as being anticipated by Peeters (USPN 6,762,056 issued Jul. 13, 2004, effective filing date May 16, 2001).

The claimed invention is drawn to visualizing and identifying an individual chain molecule uprightly disposed relative to the plastic substrate surface by probing with a scanning probe microscope in solution. As discussed below Peeters teaches detecting individual protein molecule on the plastic substrate surface using an atomic force microscope in solution.

Regarding claim 1, Peeters teaches a molecular detection method comprising a substrate 1, wherein surface is coated with coating 2 having random topology further comprising adsorption sites 10 for binding a protein containing columns 5, bumps 3, ridges, and spikes 4, which are uprightly disposed relative to the substrate surface (Fig. 1, column 9, lines 52-63, column 10, lines 4-12) and further teaches that the substrate surface comprises plastic substrate surface (column 15, lines 43-49). It is noted that the open claim language “comprising” can include other material on the surface such as coating on the plastic surface taught by Peeters.

Peeters also teaches that a protein 15 is adsorbed (i.e., immobilized) on the adsorption site 10 having topology complementary to column, ridges and spikes

uprightly disposed relative to the surface (Fig. 2 and column 10, lines 17-34). The protein 15 of Peeters is the individual chain molecule as defined in the instant claim 3.

Peeters also teaches the visualizing and identifying the a protein molecule (i.e., individual chain molecule) immobilized on the substrate surface by probing with the atomic force microscope (AFM), or scanning tunneling microscope (STM) in solution (i.e., fluid covering the test surface) so as to observe a profile of the substrate surface having individual protein molecule 15 immobilized thereon (Fig. 3 and column 8, lines 8-17, column 10, lines 35-65 and column 13, lines 31-54). The AFM and the STM of Peeters are the scanning probe microscopes as recited in the instant specification (USPGPUB paragraph 0075).

Regarding claim 2, as described above in the rejection of claim 1, Peeters teaches that the protein molecule 15 immobilized on the plastic substrate surface 1 having topology complementary to column, ridges and spikes uprightly disposed relative to the surface (Fig. 2 and column 10, lines 17-34) and is the uprightly disposed single strand molecule as defined in the instant claim 3.

Regarding claim 3, Peeters teaches a protein molecule uprightly disposed on the substrate (Fig. 2 and column 10, lines 17-22) and is the uprightly disposed single strand molecule as defined in the instant claim.

Regarding claim 4, Peeters teaches that the protein chain molecule immobilized on the substrate surface 1 in upright position (i.e., single strand molecule) forms a complex with antibody molecule (column 16, lines 42-64), thus teaching surface is multiple strand molecule formed by protein and an antibody.

Regarding claim 5, Peeters teaches that the multiple strand molecules are a complex of a protein and an antibody (column 16, lines 42-43).

Regarding claim 6, Peeters teaches mapping and measuring the number of adsorption sites occupied by the protein on the surface area of the substrate (Figs. 5 and 6 and column 11, lines 49-67 and column 12, lines 1-23), which encompasses detecting g a molecule comprises counting the number of detected protein chain molecules per unit area.

Regarding claim 7, Peeters teaches mapping and measuring the number of adsorption sites occupied by the protein on the surface area of the substrate to obtain molecular localization information of the protein molecule on the substrate surface (Figs. 5 and 6 and column 11, lines 49-67 and column 12, lines 1-23).

Regarding claim 17, Peeters teaches a production process for a substrate with a chain molecule immobilized thereon, the production process as recited in claim 1 (Figs. 1 and 2 and column 9, lines 52-67 and column 10, lines 1-34).

Regarding claim 28, Peeters teaches that the substrate 1, wherein surface is coated with coating 2 having random topology further comprising adsorption sites 10 for binding a protein containing columns 5, bumps 3, ridges, and spikes 4, which are uprightly disposed relative to the substrate surface, which are substantially perpendicular to from the substrate surface (Fig. 1, column 9, lines 52-63, column 10, lines 4-12) and further teaches the substrate is a plastic (column 15, lines 42-47).

Regarding claim 29, Peeters teaches that the profile is observed using atomic force acting between the substrate surface having the individual protein chain molecules

immobilized thereon and a probe of the AFM (Fig. 3 and column 9, lines 34-38 and column 10, lines 46-55).

Regarding claim 30, Peeters teaches that the profile is observed using AFM and further teaches that the AFM detects atomic scale features based on the force or the atomic interactions between the features present against a very fine tip of the AFM on the microcantilever, which measures the interaction by measuring an amount of flexing of the probe caused by the force between feature on the surface and the probe (column 9, lines 34-51).

Regarding claim 32, Peeters teaches a protein chip (column 23, line 34).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-7, 17, 19, 21-25 and 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al (Nano Letters, 2002, 2, 863-867) in view of Obremski et al (USPGPUB 2002/0001853 published Jan. 3, 2002) and further in view of Henderson-2 et al (USPGPUB 2002/0042081 published Apr. 11, 2002).

It is noted that Henderson et al reference cited in this rejection is different from the one cited in the previous action and referred to as Henderson-2 et al.

Regarding claim 1, Liu et al teaches a molecular detection method comprising visualizing and identifying chain molecule (Figs. 4A and 4G, pg. 865, column 2, paragraph 3) immobilized on a substrate and immobilized being uprightly disposed relative to said substrate (Fig. 1, pg. 865, column 1, paragraph 1, pg. 866, column 2, paragraph 1, lines 3-6) by probing with scanning probe microscope in solution so as to observe profile of the chain molecules immobilized on the substrate surface (Abstract, Figs. 3A and 4A, pg. 865, column 2, paragraph 2). Liu et al do not teach about plastic substrate and visualizing and identifying an individual chain molecule on the plastic substrate surface.

Regarding claim 2, Liu et al teaches that chain molecule (i.e., single stranded DNA) is immobilized on the gold surface (Fig. 2C, pg. 864, column 1, and last paragraph) and is an uprightly disposed single stranded DNA molecule (i.e., stand up configuration, pg.865, column 1, paragraph 1).

Regarding claim 3, Liu et al teaches that the uprightly single strand molecule is a nucleic acid (Fig. 1, pg. 865, column 1, and paragraph 1).

Regarding claim 4, Liu et al teaches that the chain molecule is in stand up position (Fig. 1, pg. 865, column 1, paragraph 1) and the binding of DNase I molecule to the uprightly disposed chain molecule comprises multi-strand molecule.

Regarding claim 5, Liu et al teaches that the multiple strand molecules are a complex of single strand DNA and protein DNaseI (pg. 865, column 2, paragraphs 2 and 3, pg. 866, column 1, paragraph 1).

Regarding claims 6 and 7, Liu et al teaches the imaging of single strand DNA on the substrate surface (i.e., visualizing) and further teaches that the 80.5 nm2 area contains 26 molecules (Fig. 3E, lane a2, area indicated by an arrow, pg. 865, column 1 and paragraph 2), thus teaching counting the number of detected nucleic acid molecules (i.e., chain molecules) per unit area (limitation of claim 6). Liu also teaches that number of nucleic acid molecules identifies the smallest DNA dot on the substrate surface (pg. 865, column 1, paragraph 2), which encompasses giving molecular localization information (limitation of claim 7).

Regarding claim 17, Liu et al teaches a production process for immobilizing the single stranded DNA, i.e., chain molecule on a substrate (Fig. 2, substrate – labeled as Au (III), pg. 864, column 1, paragraph 4) and further teaches that the immobilized single strand DNA is in uprightly disposed position (Fig. 1, pg. 865, column 1, paragraph 1).

Regarding claim 19, Liu et al teaches a molecular detection method comprising visualizing and identifying chain molecule (Figs. 4A and 4G, pg. 865, column 2,

paragraph 3) immobilized on a substrate and as immobilized being uprightly disposed relative to the substrate so as to observe a profile of the substrate surface having chain molecule immobilized there on (Figs. 1 and 4C, pg. 865, column 1, paragraph 1) by probing with scanning probe microscope in solution (Abstract, Figs. 3A and 4A, pg. 865, column 2, paragraph 2), wherein the molecule immobilized on the substrate is a nucleic acid (Fig. 2, pg. 864, column 1, paragraph 3). Liu et al do not teach about plastic substrate and visualizing and identifying an individual chain molecule on the plastic substrate surface.

Regarding claim 21, Liu et al teaches that the chain molecule is in stand up position (Fig. 1, pg. 865, column 1, paragraph 1) and the binding of DNase I molecule to the uprightly disposed chain molecule comprises multi-strand molecule.

Regarding claim 22, Liu et al teaches that the multiple strand molecules are a complex of single strand DNA and protein DNaseI (pg. 865, column 2, paragraphs 2 and 3, pg. 866, column 1, paragraph 1).

Regarding claims 23 and 24, Liu et al teaches the imaging of single strand DNA on the substrate surface (i.e., visualizing) and further teaches that the 80.5 nm2 area contains 26 molecules (Fig. 3E, lane a2, area indicated by an arrow, pg. 865, column 1 and paragraph 2), thus teaching counting the number of detected nucleic acid molecules (i.e., chain molecules) per unit area (limitation of claim 23). Liu also teaches that number of nucleic acid molecules identifies the smallest DNA dot on the substrate surface (pg. 865, column 1, paragraph 2), which encompasses giving molecular localization information (limitation of claim 24).

Regarding claim 25, Liu et al teaches a production process for immobilizing the single stranded DNA, i.e., chain molecule on a substrate (Fig. 2, substrate – labeled as Au (III), pg. 864, column 1, paragraph 4) and further teaches that the immobilized single strand DNA is in uprightly disposed position (Fig. 1, pg. 865, column 1, paragraph 1).

Regarding claims 27 and 28, Liu et al teaches that the molecule, as immobilized, is uprightly disposed relative to the substrate so as to extend substantially perpendicularly from said substrate surface (Figs. 1 and 3A, pg. 865, column 1, paragraph 1, lines 2-4).

Regarding claims 29 and 33, Liu et al teaches that the profile is observed using frictional force acting between the substrate surface having the individual chain molecules immobilized thereon and a probe of the scanning probe microscope (Compare the profile Fig. 4C versus 4H and pg. 866, column 1, paragraph 1). Liu et al also teaches the interaction between the methyl group and the AFM tip corresponds to a frictional force (pg. 866, column 1, paragraph 1, lines 23-28), which is reasonably interpreted as atomic force in view of lack of limiting definition for “atomic force” in the instant specification.

Regarding claims 30 and 34, Liu et al teaches that the profile is observed by measuring an amount of single stranded DNA left after the DNase I digestion caused by interaction between said DNA and DNAse I (paragraphs 0051-0054). The force required to digest single strand DNA by DNase I of Liu et al is reasonably interpreted as atomic force in view of lack of limiting definition for “atomic force” in the instant specification.

Regarding claim 31, Liu et al teaches that the substrate having a chain molecule immobilized there on is a DNA chip (Fig. 2C)

Regarding claim 32, Liu et al teaches selective immobilization of proteins on the substrate surface (pg. 863, column 2, paragraph 1, lines 15-19) and is protein chip as recited in the instant specification (USPGPUB paragraph 0063).

As described above, regarding claims 1 and 19, Liu et al do not teach the plastic substrate. However, a plastic substrate for immobilizing chain molecules was known in the art at the time of the claimed invention was made as taught by Obremski et al.

Obremski et al teaches an assay method comprising a plastic substrate (paragraph 0038) for immobilizing oligonucleotide probe (paragraph 0010). Obremski et al also teaches that the molecules immobilized on the plastic substrate stand up "vertically" from the surface (paragraph 0071). Obremski et al also teaches that the plastic surface is optically transparent, has a higher refractive index than water, easy to configure to different dimensions and amenable for chemical coupling and is well suited for molecular detection by AFM and evanescent wave excitation method (paragraphs 0038 and 0071).

As described above, Liu et al teaches a method comprising gold surface to immobilize the DNA molecule in upright position suitable for AFM scanning. Obremski et al teaches immobilizing the molecules vertically (i.e., in upright position) on a plastic substrate and further teaches advantages of using a plastic substrate for immobilizing the DNA for AFM scanning. Since both gold and plastic substrates are compatible for

AFM scanning, use of plastic substrate for immobilizing individual chain molecule is obvious over Liu et al and Obremski et al.

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to modify the substrate of Liu et al with the plastic substrate of Obremski et al with a reasonable expectation of success.

An artisan would have been motivated to modify the substrate of Liu et al with the expected benefit of having a plastic surface, that is optically transparent, easy to configure to different dimensions and amenable for chemical coupling and is well suited for molecular detection by AFM and evanescent wave excitation as taught by Obremski (paragraphs 0038 and 0071).

Regarding claims 1 and 19, Liu et al teaches the visualizing and calculating about 26 molecules in an 80.5 nm2 area (Fig. 3E, lane a2, area indicated by an arrow, pg. 865, column 1 and paragraph 2). Obremski et al also teaches an AFM scanning of immobilized avidin array and further teaches that avidin extends 200 nm vertically from the surface and binds to biotin (paragraph 0071). Liu et al and Obremski et al do not teach visualizing and identifying an individual chain molecule by scanning probe microscope. However, visualizing and identifying an individual chain molecule by scanning probe microscope was known in the art at the time of the claimed invention was made as taught by Henderson-2 et al.

Henderson-2 et al teaches a method for detecting molecular interaction between an object and a surface comprising the steps of affixing the a plurality of object 12 on the substrate surface 10 (viz., Fig. 4a) and detecting the location and size of the object

12 by scanning the entire surface image using AFM in solution (Fig. 1b and Example 1 and paragraphs 0037- 0038, 0041 and 0046). Henderson-2 et al also teaches that the substrate comprises polystyrene (paragraph 0066), which is a plastic as defined by Obremski et al (paragraph 0038). Henderson-2 et al also teaches that the "utilization of an AFM to run a scan is well known to those skilled in the art and enables the user to determine the location of the objects on the surface" (paragraph 0038). Henderson-2 et al further teaches that the object 12 further comprises a first object and a second object bound together on the surface consists of nucleic acid and a complementary nucleic acid (paragraph 0046). Henderson et al also teaches locating the objects using AFM and characterizing the force necessary for separating the first and second objects based on the AFM probe deflection (paragraphs 0043-0046), which also encompasses visualizing individual objects. Combined teaching of Henderson-2 et al of detecting the location and size of an object (i.e., nucleic acid molecule on the substrate surface) encompasses visualizing (i.e., imaging) and detecting (i.e., size) of an individual molecule (i.e., object). Henderson-2 et al also teaches that the AFM imaging allows for rapid and inexpensive screening of large number of binding interactions for categorizing and characterizing the binding affinity between two interacting molecules (paragraph 0021).

As described above, Liu et al teaches imaging of nucleic acids using AFM in solution. Henderson-2 et al teaches a method step of imaging the surface (i.e., visualizing) and detecting (i.e., identifying) surface bound molecules using AFM in solution for rapid and inexpensive way screening for molecular interactions between two

binding partners including nucleic acids (paragraphs 0021 and 0046). Henderson-2 et al further teaches that the AFM scanning in solution is also routinely practiced in the art and one having the skill in the art able to locate and identify molecules on the surface (paragraph 0038). Therefore claimed method steps of visualizing, identifying an individual chain molecules on a plastic substrate are obvious over Liu et al, Obremski et al and Henderson-2 et al.

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to modify the visualizing and identifying step of Liu et al with the method of step visualizing and identifying individual object on the surface of Henderson-2 et al with a reasonable expectation of success.

An artisan having the ordinary skill in the art would have been motivated to modify the visualizing and identifying step of Liu et al with the expected benefit of a rapid and inexpensive screening of large number of binding interactions for categorizing and characterizing the binding affinity between two nucleic acid molecules as taught by Henderson -2 et al (paragraph 0021). Teachings of Henderson et al would be beneficial to Liu et al for properly selecting nucleic acid probes for the fabrication of DNA biosensors, biochips and engineering of biostructures as desired by Liu et al (pg. 866, column 2 and paragraph 1).

Response to Remarks from the Applicants

Claim rejections under 35 U.S.C. § 102(e)

14. Applicant's arguments filed on April 12, 2010 with respect to claims 1-7, 17, 28-30 and 32 as being anticipated by Henderson et al have been fully considered (Remarks, pgs. 10-12). These arguments are directed to the reference of Henderson et al is not available as prior art. The reference of Henderson is withdrawn from further considerations in view of Applicant's arguments and establishing the effective filing date of the instant claims to April 18, 2003.

Claim rejections under 35 U.S.C. § 103(a)

15. Applicant's arguments filed on April 12, 2010 with respect to claims 1-5, 17, 19, 21, 22 and 25-34 as being obvious over Liu et al, Obremski et al and Seong et al have been fully considered (Remarks, pgs. 12-22). Applicant's arguments regarding teachings of Seong et al are persuasive (Remarks, pgs. 20 and 21). The reference of Seong et al is withdrawn from further consideration. As discussed above in section 13, claimed method steps are obvious over Liu et al, Obremski et al and Henderson-2 et al. Applicant's arguments as it pertains to the teachings of Liu et al and Obremski et al used in this office action are discussed below.

Applicants reiterate the previous argument that one of ordinary skill in the art would not observe the molecules individually so as to produce the nanopatterns consisting of DNA molecules (Remarks, pg. 17, paragraph 2). Applicants further assert that Liu would not suggest "molecular detection methods" and visualizes and identifies the aggregates of the thiolated ssDNA molecules (Remarks, pg. 18, paragraph 1). These arguments are not persuasive because Liu et al teaches "structure of the

nanopattern and the relative orientation of the single stranded DNA in situ using AFM and further teaches that the DNA molecules have stand up orientation" (pg. 866, column 2, lines 3-6). Furthermore, Applicants have provided any factual evidence to support the asserted "not observing the nanopatterns of the DNA molecules by AFM" or visualizing and identifying the aggregates. As described above in section 13, steps of visualizing identifying single object (molecule) are taught by Henderson-2 et al. For above reasons arguments are not persuasive.

Applicants further argue that teachings of Obremski et al were to properly combine with the teachings of Liu et al would have neither disclosed nor would have suggested the presently claimed invention, viz., visualizing and identifying an individual chain molecule immobilized on the substrate (Remarks, pg. 19, paragraph 2). These arguments are not persuasive because as described above in section 13, teachings of Obremski et al is relied for a plastic substrate. It is maintained that Liu et al teaches visualizing and identifying nucleic acid molecule immobilized on the surface and as discussed above Henderson-2 et al teaches visualizing and identifying single molecule on the surface.

Applicant's arguments with respect to claims 1-3, 6-7, 19, 23-24 and 27-28 being obvious over Lee in view of Obremski have been fully considered (Remarks, pgs. 22-23). These arguments are moot in view of withdrawn rejections and new grounds of rejection necessitated by claim amendments.

Applicants remaining arguments reiterate the arguments made before for teachings of Liu et al, Obremski et al and Seong et al (Remarks, pgs. 24 and 25). These arguments are not persuasive for the same reasons as described above.

Conclusion

16. No claims are allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Narayan K. Bhat whose telephone number is (571)-272-5540. The examiner can normally be reached on 8.30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571)-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Narayan K. Bhat/

Examiner, Art Unit 1634

/Stephen Kapushoc/

Primary Examiner, Art Unit 1634